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10/066,546	01/30/2002	Richard N. Ellson	7610-0042.20	3901

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EXAMINER
BERMAN, JACK I

ART UNIT	PAPER NUMBER
2881	

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/066,546	Applicant(s) ELLSON ET AL.	
	Examiner Jack I. Berman	Art Unit 2881	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-161* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-161* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5, 6, 7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 79-87 and 152-154 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claim 79, the term "optionally" renders the claim indefinite because it is unclear whether the limitation(s) following the term are part of the claimed invention. See MPEP § 2173.05(d). This ambiguity is also contained in dependent claims 80-87. Claims 152 and 153 both recite the limitation "[t]he method of claim 141, wherein the plurality of droplets is deposited..." in line 1. There is insufficient antecedent basis for this limitation in the claim because the only antecedent basis for "the plurality of droplets" is in claim 151, not 141. For purposes of examination, claims 152 and 153 were both examined on the assumption that they were intended to depend from claim 151, but the claims must be corrected. Similarly, the only antecedent basis for "the different designated sites" in line 1 of claim 154 is in claim 153, not claim 143 as is written. Again, claim 154 was examined on the assumption that it was intended to depend from claim 153, but the claim must be corrected.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 5, 6, 9-11, 16-25, 29-34, 36, 37, 39, 40, 46-66, 69, 72-86, 145, and 151-155 are rejected under 35 U.S.C. 102(e) as being anticipated by Williams et al. Williams et al. discloses a method of preparing a plurality of analyte molecules for analysis comprising preparing an array of samples on a substrate (which may comprise a plurality of wells on the substrate or an array of discrete locations on a flat substrate as is indicated at paragraphs [0028] and [0029]) by applying focused acoustic energy through a coupling fluid to each sample reservoir to cause the ejection of droplets. At the last 9 lines in paragraph [0033], Williams et al. teaches:

> "In some embodiments of the present invention, it may be desirable to direct a fluid droplet to a measuring device or other remotely located zone, thus, the target may not comprise a tangible object but instead comprise a collection zone defined by a containment field, a conduit, a chamber, a collector, a container, or the like. In this manner, a droplet of fluid could be directed, for example, to a conduit that leads to the reaction chamber of a mass spectrometer, or the like."

The "reaction chamber" of a mass spectrometer is inherently an ionization chamber because all mass spectrometers measure the mass of molecules by ionizing them in an ionization chamber and measuring their charge-to-mass ratios by means of electric and/or magnetic fields. In paragraph [0032], Williams et al. teaches that the wells of a micro-titer plate are suitable for use as the reservoirs of the sample fluid. The last three lines of this paragraph state: "One example of a suitable plate is a 1536 well plate (e.g., catalog number 3950 available from Coming Corporation)." According to Corning's on-line product guide (Coming appears to be a typographical error), each well of the 3950 model 1536-well plate contains a maximum volume of 2 μL of fluid. According to paragraph [0052] of the published application, "the defined droplet diameter is in the range of about 1 micrometer to about 10,000 micrometers." Assuming the

minimum diameter of 1 micrometer for each of the ejected droplets and a spherical shape for the droplets (the natural shape for droplets), basic geometric calculations (volume = $4/3\ \pi\ r^3$ where r is the radius) give a droplet volume of 0.5 fL. In paragraphs [0059-0062], Williams et al. teaches that the source fluid may be a biomolecule, which may be either nucleotidic or peptidic. Williams et al. also teaches, in paragraph [0080], to detect reflected acoustic radiation to monitor the volume of sample in each reservoir. In paragraph [0039], Williams et al. teaches that means may be provided to charge the fluid sample and a charged surface (an electrode) provided to accelerate the droplet (which inherently involves either attraction or repulsion). Paragraph [0040] goes on to teach to establish an electric field across the trajectory of the droplets in order to deflect them. The sample vessel that receives the droplets and the reservoir in the Williams et al. system are both inherently portions of microfluidic devices because they handle microscopic quantities of fluids. In paragraphs [0041-0042], Williams et al. teaches to repeat the acoustic pulses to individually eject identically sized droplets. The trajectories of these droplets would inherently be identical because each droplet is subjected to identical forces. In paragraph [0057], Williams et al. teaches:

> "Because these methods may be employed in high throughput applications, it is preferred that methods of the invention further comprise user-defined positioning of the acoustic liquid deposition emitter relative to an array of source wells, thus providing for user-defined association of the acoustic liquid deposition emitter with a selected pool of source fluid for ejection of a droplet therefrom. This can be accomplished by a variety of methods. For example, in the case where a multi-well plate is employed as the source fluid containment structure, a computer-controlled translator (e.g., an actuator, or the like) can manipulate the position of the multi-well plate or a movable stage upon which the multiwell plate rests. Thus, a selected well or a selected succession of wells is placed over the acoustic deposition emitter, as the source fluid contained in each well is needed for the application being conducted (e.g., oligonucleotide synthesis, or the like). In a related embodiment, the acoustic deposition emitter may be moved rather than the source plate. For example, the source fluid

> containment structure may remain fixed in position and the acoustic liquid deposition emitter may be moved relative to a well or particular source fluid of interest contained in or on the source fluid containment structure."

In paragraph [0028], Williams et al. teaches that the reservoirs may be formed on a flat substrate as well as a multiwell plate. In paragraphs [0063-0070] Willams et al. teaches that analysis-enhancing fluids such as labels may be used as the source fluid and in paragraph [0070] further teaches that the droplets can be directed to an array of sites on the target.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4, 7, 8, 12-15, 26-28, 38, 41-44, 67, 68, 70, 71, 87-106, 112-125, 135-144, and146-148 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al. As is discussed above, Williams et al. discloses a method of preparing a plurality of analyte molecules for analysis comprising preparing an array of samples on a substrate by applying focused acoustic energy to each sample reservoir to cause the ejection of droplets that may then be directed through a conduit to a mass spectrometer. Williams et al. does not specify the type of mass spectrometer used. It would therefore have been necessary for a person having ordinary skill in the art to look to known mass spectrometers to find one to use in the Williams et al. system. Both time-of-flight mass spectrometers and quadrupole analyzers (which inherently comprise charged surfaces during operation in order to produce the electric fields required for mass analysis) are well known in the art. It would have been obvious to a person having ordinary

skill in the art to use one of these known mass spectrometers as the nominally recited mass spectrometer cited in the Williams et al. application. Since one of the stated uses of the Williams et al. apparatus is to direct droplets to a mass spectrometer for analysis, the nature of the fluid sample, i.e. its volume, its composition (including any carrier fluid that may be provided), its molecular weight, its volatility or freezing point (which would determine whether it evaporated from the target surface or solidified on the target surface), the percentage of the total sample fluid in each droplet, and the amount of the fluid ejected, is, by definition, a matter for routine experimentation. The size of the conduit leading from the sample reservoir, or even the omission of the conduit altogether so that the reservoir was located in the ionization chamber itself instead of in an adjoining chamber, and the size of the ionization chamber would also have been obvious matters for routine experimentation which a person having ordinary skill in the art would adjust in accordance with the amount of sample fluid to be analyzed and the strength of the vacuum required by the mass spectrometer. It would have been obvious to a person having ordinary skill in the art that the diameter of any opening between the sample reservoir and the ionization chamber (or any other sample vessel) would have to be greater than the diameter of the droplets formed so as maintain the non-contact aspect of Williams et al.'s acoustic fluid transfer method emphasized in the abstract of the application. If the opening diameter was equal to or less than the droplet diameter, contact between the conduit walls and the droplet could not possibly be avoided. It follows that, since Williams et al. teaches at paragraphs [0050-0052] that the diameter of the droplets produced can be controlled by appropriate selection of the wavelength of the acoustic wave used to cause ejection, the wavelength of the acoustic wave used to cause ejection of the droplets should be selected on the basis of the size of the opening because that would limit

the size of the droplets to be formed. At paragraphs [0081-0082], Williams et al. further teaches that the parameters used to control the acoustic wave, including frequency (which is directly related to the wavelength) should be adjusted in accordance with the depth of the fluid samples. While Williams et al. teaches, in paragraph [0039], that means may be provided to charge the fluid sample, the application does not teach whether the charging of the plurality of fluid samples described should be successively or simultaneously; however, since these are the only two possibilities, the choice of which of the two to use would have been an obvious matter for routine experimentation. Williams et al. does not specify how the plurality of source reservoirs are filled, but it would have been obvious to a person having ordinary skill in the art to use the acoustic ejection technique disclosed in the application to fill them because the technique is designed to transfer small amounts of fluid to designated sites on a substrate, exactly the situation involved in filling the plurality of reservoirs in Williams et al.'s "source fluid containment structure".

Claims 107-111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al. as applied to claims 4, 7, 8, 12-15, 26-28, 38, 41-44, 67, 68, 70, 71, 87-106, 112-125, 135-144, and146-148 above, and further in view of Whitehouse et al. Williams et al. does not specify the structure of the conduit leading to the mass spectrometer. Whitehouse et al. teaches at line 62 in column 4 through line 28 in column 5 that it is better to introduce ions into a mass spectrometer through a glass capillary with metalized ends to which different potentials are applied, thereby generating an electric field, than it is to introduce the ions through a simple orifice. It would therefore have been obvious to a person having ordinary skill in the art to use Whitehouse et al.'s capillary as Williams et al.'s conduit.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and

useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 126-133 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 105-112 of copending Application No. 09/784,705 because the focused acoustic energy claimed in claims 126-133 of the instant application will inherently cause the ejection of droplets from each of the fluid reservoirs to which it is applied in the same way that it does in claims 105-112 of 09/784,705. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 134 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 29 of copending Application No. 09/784,705. Although the conflicting claims are not identical, they are not patentably distinct

from each other because it would have been obvious to a person having ordinary skill in the art to use the mass spectrometer into which the ionized analyte molecules are introduced in claim 29 of 09/784,705 to determine their mass since that is the purpose of mass spectrometers.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 145-150, 154, 155, and 156-159 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-25, 37, 43, 28-31 respectively, of copending Application No. 10/087,372. Although the conflicting claims are not identical, they are not patentably distinct from each other because the surface of the cell sample onto which the analysis-enhancing fluid is directed in claims 20-25, 37, 43, and 28-31 of 10/087,372 constitutes "a sample surface for analysis" as is claimed in claims 145-150, 154, 155, and 156-159 of the instant application.

.This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 151-153 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33-35 of copending Application No. 10/087,372 in view of claim 20 of that same application. It would have been obvious to a person having ordinary skill in the art to form the droplets claimed in claims 33-35 of 10/087,372 from the analysis-enhancing fluid claimed in claim 20 of that application (by way of its dependency from claim 7) and to subject the sample to conditions effective to allow the analysis-enhancing fluid to interact with the sample surface so as to render the sample surface suitable for analysis in the manner further claimed in claim 20.

This is a provisional obviousness-type double patenting rejection.

Claims 160 and 161 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hadimioglu et al. in view of Swierkowski. Hadimioglu et al. discloses a microfluidic device (60) (illustrated in Figures 2 and 3) comprising a base (70), a cover plate (lid 44), a microconduit (reservoir connect 66) defined by the base surface and the cover plate, the microconduit fluidly communicating with an inlet opening (68) and an outlet opening (45), an ejector comprising an acoustic radiation generator (transducer 16) for generating acoustic radiation, and a focusing means (22) for focusing the acoustic radiation at a focal point near the surface of a fluid (40) at the outlet opening (45). At lines 6-13 in column 3, Hadimioglu teaches:

> "In operation, energization of transducer 16 emits an acoustic wave which travels through substrate 20 to Fresnel lens 22. The lens produces a focused acoustic energy wave 39 that passes through acoustic coupling fluid 24 and membrane 36, reaching an apex at biofluid meniscus surface 40 of biofluid 38. Supplying of the focused energy to surface 40 causes disruptions in the surface, resulting in ejection of a biofluid drop 42 from the cartridge 12 to substrate 43."

This particular section of Hadimioglu is directed to the embodiment illustrated in Figure 1, but the embodiment illustrated in Figures 2 and 3 operates in the same way to use acoustic radiation focused on the surface of the biofluid to cause the ejection of drops through the outlet opening (45) of the microfluidic device (60). The operational connection of the acoustic radiation generator (16) to the base (70) inherently comprises some means to position it in acoustic coupling relationship. Hadimioglu does not teach to form the required microconduit (66) as a microchannel formed in a surface of the base with the cover plate and microchannel cooperating to form the microconduit. Swierkowski, on the other hand, does teach to form microconduits suitable for use in acoustically driven microfluidic devices as microchannels (micro-capillaries 12, 13, 14, 15) in a substrate (10) that cooperate with a cover plate (member 11). The use of

Swierkowski's cooperating microchannels and cover plate to form the microconduit (66) required by Hadimioglu instead of Hadimioglu's lid (44) that has a portion projecting toward the base (70) would have been an obvious substitution of equivalent parts.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jack I. Berman whose telephone number is (703) 308-4849. The examiner can normally be reached on M-F (8:30-6:00) with every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John R. Lee can be reached on (703) 308-4116. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9318 for regular communications and (703) 872-9319 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0956.

Jack I. Berman
Primary Examiner
Art Unit 2881

jb
May 28, 2003